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20306 7590 12/12/2007 MCDONNELL BOEHNEN HULBERT & BERGHOFF LLP 300 S. WACKER DRIVE 32ND FLOOR CHICAGO, IL 60606			EXAMINER KISHORE, GOLLAMUDI S	
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**BEFORE THE BOARD OF PATENT APPEALS
AND INTERFERENCES**

MAILED

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GROUP 1600

Application Number: 09/155,605
Filing Date: September 29, 1998
Appellant(s): DE VRINGER ET AL.

Michael S. Greenfield
For Appellant

EXAMINER'S ANSWER

This is in response to the appeal brief filed 10-16-07 appealing from the Office action
mailed 4-16-07.

(1) Real Party in Interest

A statement identifying by name the real party in interest is contained in the brief.

(2) Related Appeals and Interferences

The examiner is not aware of any related appeals, interferences, or judicial proceedings which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) Status of Claims

The statement of the status of claims contained in the brief is correct.

(4) Status of Amendments After Final

The appellant's statement of the status of amendments after final rejection contained in the brief is correct.

(5) Summary of Claimed Subject Matter

The summary of claimed subject matter contained in the brief is correct.

(6) Grounds of Rejection to be Reviewed on Appeal

The appellant's statement of the grounds of rejection to be reviewed on appeal is correct.

(7) Claims Appendix

The copy of the appealed claims contained in the Appendix to the brief is correct.

(8) Evidence Relied Upon

EP 0521 562	De VRINGER	1-1993
EP 0687 295	CITERNESI	10-1995
EP 0159 237	LAFON	10-1985
GB 2002 319	SCHNEIDER	2-1979
JP 05194253	HIROSHI	8-1993
5,693,516	BLINKOVSKY	12-1997

(9) Grounds of Rejection

The following ground(s) of rejection are applicable to the appealed claims:

1. Claims 1-9, 12-17 and 19-37 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0 521 562 of record.

EP 0521 562 teaches instant reverse vesicles containing sucrose fatty acid esters and an apolar vehicle, which is a silicone oil or isoparaffin. The compositions further contain a lipophilic stabilizing factor such as cholesterol and an active agent. The process of preparation involves making a dispersion of reversed vesicles from the non-ionic surfactants and the active agent in an apolar (non-polar) vehicle such as volatile silicone oil and removing the non-polar vehicle (note the abstract, col. 5, line 49 through col. 12, line 56, Examples and claims). Although EP does not explicitly teach that the preparation is in the form of a powder, since it teaches on col. 12, lines 55-56, the removal of the non-polar vehicle (volatile silicon oil), the teachings of a powder form of the preparation are implicit in the reference.

2. Claims 1-9, 12-17 and 19-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0521562 by itself or in further combination with EP 0 678 295 (Citernes), EP 0159237 (Lafon), GB 2002319 (Schneider) , JP 05194253 (Hiroshi) by themselves or in combination (all are of record).

According to instant claims, the preparation is a reversed vesicle, meaning that the hydrophobic group of the surfactant molecule is oriented toward the hydrophobic continuous medium, which is oil (silicone oil).

As pointed out above, EP 0521 562 teaches instant reverse vesicles containing sucrose fatty acid esters and an apolar vehicle, which is a silicone oil or isoparaffin. The compositions further contain a lipophilic stabilizing factor such as cholesterol, a hydrophilic stabilizing factor, and an active agent. The process of preparation involves making a dispersion of reversed vesicles from the non-ionic surfactants and the active agent in an apolar (non-polar) vehicle such as volatile silicone oil and removing the non-polar vehicle (note the abstract, col. 5, line 49 through col. 12, line 56, Examples and claims). What this reference lacks are the explicit teachings that the preparation is in the powder form.

EP 0678 295 teaches that vesicular preparations (hydrophilic group of the lipid is oriented towards the continuous external phase (water) can be lyophilized to form powders (note Example 1 and claims 1 and 7).

EP 0159237 teaches that emulsions (micelles) can be freeze-dried to form powders, which are easier to handle than emulsions (note the abstract).

GB teaches that dehydration of lipid vesicles (liposomes) to prepare a stable powder, which can be stored for longer periods of time (note the abstract).

JP 05194253 teaches the preparation of a powder of reverse micelles containing a surfactant (note the abstract).

Assuming that the preparations taught by EP 0521 562 are not powder preparations, it is deemed obvious to one of ordinary skill in the art that if the removal of the external medium in which the vesicles are dispersed results in a powdery preparation as evidenced by the references of the references of EP 295, EP 237 and JP 253. One of ordinary skill in the art would be motivated to remove the external medium such as volatile silicone oil and prepare the powders since GB teaches that powders are stable and can be stored for longer periods of time.

3. Claims 1-9, 12-17 and 19-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over EP 0521562 in combination with Blinkovsky.

As pointed out above, EP 0521 562 teaches instant reverse vesicles containing sucrose fatty acid esters and an apolar vehicle, which is a silicone oil or isoparaffin. The compositions further contain a lipophilic stabilizing factor such as cholesterol, a hydrophilic stabilizing factor, and an active agent. The process of preparation involves making a dispersion of reversed vesicles from the non-ionic surfactants and the active agent in an apolar (non-polar) vehicle such as volatile silicone oil and removing the non-polar vehicle (note the abstract, col. 5, line 49 through col. 12, line 56, Examples and

claims). What this reference lacks are the explicit teachings that the preparation is in the powder form.

Blinkovsky discloses dried preparations of reverse micelles containing surfactants (abstract, col. 1, line 66 through col. 3, line 53, examples and claims).

It would have been obvious to one of ordinary skill in the art to remove the solvent and prepare the composition of EP in a powder form with a reasonable expectation of success since Blinkovsky teaches that dried preparations of reverse micelles can be made by evaporating the external medium.

(10) Response to Argument

Rejection 1:

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant continues to argue that although DeVringer instructs to remove the non-polar excipients to obtain an instant preparation, DeVringer fails to teach a method for doing so and without a teaching of how to remove the non-polar vehicle, the ordinary artisan could not arrive at the presently claimed powder of reversed vesicles. This argument is not persuasive. The removal of organic solvents is well known in the art and especially it is within the skill of the art to realize that the silicon oil is volatile and therefore, it could be removed easily. If there were no method existing in the art for the removal of an organic solvent or non-polar excipients, DeVringer would not have instructed (applicant himself recognizes that DeVringer instructs the removal).

Therefore, applicant's arguments that the Office has not provided evidence or scientifically based reasoning that as of the time of filing the present invention one of

ordinary skill in the art would have necessarily known of and employed a method of removing non-polar vehicles that would necessarily lead not merely to a powder, but to a powder of reversed vesicles having the properties recited in the present claims are not persuasive. Applicant's arguments that not every method of removing the non-polar vehicle from the various dispersions of DeVringer will result in a powder as presently claimed are not persuasive since it is not accompanied by experimental evidence. Furthermore, according to instant specification on page 5, lines 14-25, the removal of apolar vehicle is done by either rotational evaporation or by spray drying; DeVringer teaches rotational evaporation method. In addition, as pointed out before, DeVringer teaches reversed vesicles in a non-polar medium and on col. 12, lines 46-56 clearly states, "After having obtained a dispersion of vesicles according to one of the above-mentioned method, additional production steps comprise:

- reducing the size of the vesicles by methods known in the art (sonication, extrusion, micro fluidization)
- polymerizing the vesicles in case a polymerizable surfactant is used by methods known in the art;
- ***removing the non-polar excipient(s) to obtain an instant preparation***".

This last statement in the prior art clearly implies that that the non-polar excipient is removed contrary to applicant's arguments that conventional techniques for removing the vehicles cannot be applied to reversed vesicular systems without undue experimentation.

With regard to applicant's arguments that the office has not provided evidence or scientifically based reasoning that as of the time of filing the present invention one of ordinary skill in the art would have necessarily known of and employed a method of removing non-polar vehicles that would necessarily lead not merely a powder, but to a powder of reversed vesicles having the properties recited in the present claims, the examiner points out that preparation of liposomal powders (reverse vesicles) which could be reconstituted into liposomes again upon the addition of a medium is known in the art as the prior art applied below.

Rejection 2:

Applicant's arguments have been fully considered, but are not persuasive. The examiner has already addressed applicant's arguments with regard to EP. Applicant argues the following regarding Citernes, Schneider, Lafon and Hiroshi:

"Citernes, although related to vesicular dispersion preparations, teaches a composition containing a polar external phase and not a non-polar phase, as presently claimed. Citernes relates to a completely different vesicular technology compared to the present claims. Citernes is concerned with how to load an active principal into liposomes. It is not concerned with increasing the amount of the liposome vehicle, let alone reversed vesicles in a non-polar vehicle. Citernes relates to providing a method to manufacture liposomes (vesicles in a polar vehicle) exhibiting a high drug content by the formation of a drug-phospholipid complex in an organic solvent first, removing the organic solvent, and then adding the polar vehicle to the residue thus obtained.

Schneider, like Citernes, although related to vesicular dispersion preparations, also teaches composition containing a polar external phase, not a non-polar phase. Schneider, aims at providing a solution for the short shelf life of liposomes (vesicles in a polar vehicle) by providing a process for the dehydration of the liposomes - by lyophilization in conjunction with the addition of a hydrophilic compound - to obtain a powder that can be stored for longer periods and from which, together with an aqueous medium, a liposome dispersion can be re-constituted. However, during lyophilization about 30% of the liposomes were destroyed and therefore there is a decrease in percent yield of liposomes. As Schneider deals with liposomes in a polar medium (rather than reversed vesicles in a non-polar medium) and teaches a loss of 30% of the liposomes, one of ordinary skill in the art seeking to improve the percent yield of reversed vesicles in a non-polar vehicle would not be inclined to apply the teachings of this document to this problem.

As illustrated in both Schneider and Citernes, techniques for removing an external vehicle are commonly applied to systems wherein the external phase comprises water (*i.e.*, an aqueous, polar system). Such an external phase clearly does not meet the requirements of the instant claims for a non-polar excipient or mixture of non-polar excipients. One skilled in the art would not have any expectation of success or predictability in applying any methodology related to such aqueous systems to the instant non-polar systems, and the Office has identified none.

Lafon (micelles) and Hiroshi (reverse micelles) relate to a totally different physical systems having different properties from reversed vesicular systems. The differences between micelles and vesicles has been previously discussed (see, *e.g.* Blinkovsky, Column 2, 11. 2 - 15; and the previous discussion of the differences between micelles and vesicles). One skilled in the art would not combine the teachings of such non-analogous art; nor would one skilled in the art have any expectation of success in applying any methodology related to micellar systems to the instant vesicular systems".

These arguments are not persuasive. These references are combined to show the state of the art in the preparations of powders from micelles, emulsions and liposomes (vesicles) ***and even reverse micelles*** by removal of solvents. Based on the state of the art as evident from these references and from that of De Ringer (EP 562) who teaches the reverse micelles and the removal of solvents, the preparation of powders would have been obvious to one of ordinary skill in the art with a reasonable expectation of success. The examiner has thus provided the predictability to satisfy "an element necessary for finding obviousness under KSR).

Rejection 3:

Applicant's arguments have been fully considered, but are not found to be persuasive. Applicant argues that DeVringer is concerned with the production of dispersions of vesicles while Blinkovsky is concerned with the preparation of dispersions and compositions containing reverse micelles. Applicant also argues depicting the pictures of reverse micelle and reverse vesicle that for a reversed vesicle, the interior of the bilayer forming the vesicle is polar and the outer surfaces of the bilayer are non-polar and the both the interior and exterior of the reversed vesicles are

non-polar. Applicant further argues with respect to the differences between the reverse micelles of Blinkovsky and instant vesicles on page 15 citing the reference of Kunieda. Therefore, according to applicant one skilled in the art would not have considered combining the teachings of DeVringer with Blinkovsky because they are concerned with fundamentally different problems. This argument is not persuasive since Blinkovsky is concerned with **reverse** micelles and not just micelles and because the evaporation method used in both is the same, that is, rotoevaporation (col. 6, lines 19-23). One of ordinary skill in the art would expect the evaporation of any solvent or medium including volatile oils by rotoevaporation. In this context, the examiner respectfully directs the Board's attention to page 3, lines 13-14 of instant specification which recite volatile oils as apolar vehicles. Removal of solvents is a basic skill in the highly developed art of Chemistry and Biochemistry. The primary reference of De Vringer, as pointed out above on page 7, also teaches the removal of non-polar excipients from the preparation.

(11) Related Proceeding(s) Appendix


No decision rendered by a court or the Board is identified by the examiner in the Related Appeals and Interferences section of this examiner's answer.

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For the above reasons, it is believed that the rejections should be sustained.

Respectfully submitted,

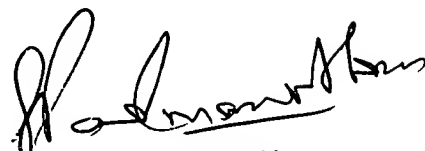

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